AD-A162 703 FINAL REPORT ON CONTRACT N00014-79-C-0522(U) MICHIGAN STATE UNIV EAST LANSING DEPT OF STATISTICS AND PROBABILITY J C GARDINER DEC 85 N00014-79-C-0522 1/1

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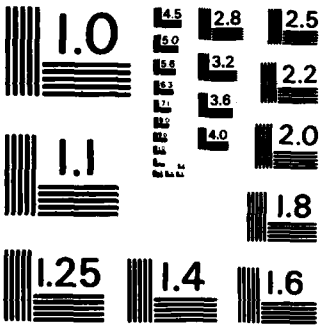

FINAL REPORT SUBMITTED TO THE

OFFICE OF NAVAL RESEARCH

ON CONTRACT N00014-79-C-0522

by

Joseph C. Gardiner
Principal Investigator

December 1985

Michigan State University

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ABSTRACT OF RESEARCH ACCOMPLISHED

ON CONTRACT N00014-79-C-0522

The research performed on this contract addressed statistical methodologies that would be appropriate in censored survival analyses and competing risks models. Both general parametric and nonparametric models were considered. The problems of efficient estimation of parameters of the underlying failure time distribution were addressed when the data may only be partly observable due to the presence of censorship. The methodogy developed permits costs associated with monitoring of experimentation and of recruitment of units to be incorporated into the basic infrastructure leading to the description and properties of optimal procedures that minimize overall expected cost. These optimal designs are inherently sequential in nature, in that the optimal stopping time or sample size is solely determined by the observed information gathered by the experimeter.

FINAL REPORT
on
ONR-Contract N00014-79-C-0522

by
Joseph C. Gardiner
Principal Investigator

This report describes the main achievements of our research efforts on the above contract. The central thesis of our research related to statistical inference problems arising in the analysis of censored data. Such data or incomplete observations arise naturally or by design in several longitudinal studies which encompass clinical trials and life-testing, reliability, demography and epidemiological investigations. Our research publications cover three broad areas: i) Sequential estimation procedures from randomly censored data ii) Properties of likelihood ratio processes arising in progressively censored data, and iii) Estimation of biometric functionals in multiple decrement models.

Listed below are the publications prepared under this contract. It is followed by a brief description of their contents and significance of the results achieved.

a) List of publications

1. Risk-efficient estimation of the mean exponential survival time under random censoring. Proc. Natl. Acad. Sci. USA, Vol. 81, pp. 5906-5909 (1984). J. Gardiner and V. Susarla.

2. Sequential estimation of the mean survival time under random censorship. Commun. Stat. Sequential Analysis Vol. 2, 201-233 (1983). J. C. Gardiner and V. Susarla.

3. Fixed-width confidence intervals of the exponential mean survival time under random withdrawals. J. Stat. Plann. & Inference, 12, 153-159 (1985). J. C. Gardiner, V. Susarla and J. van Ryzin.

4. Time-sequential estimation of the exponential mean under random withdrawals. To appear in Ann. Statist. (1986). J. C. Gardiner, V. Susarla and J. van Ryzin.

5. On the estimation of the median survival time. To appear in Inst. Math. Stat. Mono. & Lecture Notes (1986). J. C. Gardiner & V. Susarla.

6. On the asymptotic theory of estimation of the survival function in competing risks analyses. Michigan State University Research Mono. (1984). J. C. Gardiner and V. Mandrekar.

7. Weak convergence of a Bayesian nonparametric estimator of the survival function under progressive censoring. Statistics & Decisions 1, 257-268. J. C. Gardiner and V. Susarla.

8. A nonparametric estimator of the survival function under progressive censoring. Inst. Math. Stat. Mono. & Lecture Notes, Vol. 2, 26-40. (In Survival Analysis. J. Crowley, R. Johnson, editors). J. C. Gardiner and V. Susarla.

9. Local asymptotic normality of progressively censored likelihood ratio statistics and applications. J. Multivariate Analy. 12, (2) 230-247 (1982). J. C. Gardiner.

10. Convergence of progressively censored likelihood ratio processes in life-testing. Sankhya V43 I, Part A, 37-51 (1981). J. C. Gardiner.

11. Asymptotic normality of a variance estimator of a linear combination of a function of order statistics. Z. Wahrsheinlichkeitstheorie und verw. Gebiete 50, 205-221 (1979). J. C. Gardiner and P. K. Sen.

12. Properties of time-sequential statistics in life-testing. Reliability & the Acquistions Process, 1983-193. D. DePriest, R. Launer, editors. J. C. Gardiner.

13. Asymptotic normality of class of time-sequential statistics and applications. Commun. Stat. A7, 4 373-388 (1978). J. C. Gardiner and P. K. Sen.

14. The asymptotic distribution of mortality rates in competing risks analyses. Scandinavian J. Stat. Vol. 9, Pt. 1, 31-36 (1982). J. C. Gardiner.

15. Properties of occurence-exposure rates in multiple decrement theory. J. Stat. Plann. & Inference, Vol. 8, 301-314. J. C. Gardiner.

16. Bounded length sequential confidence intervals for the median survival time. Submitted for publication.

The following titles are in preparation.

17. A comparison of sequential confidence interval estimation procedures for the median survival time. A Simulation Study.

18. Risk-Efficient estimates for quantiles of the survival distribution with sampling costs.

19. The boundedness of the regret of a sequential procedure for the estimation of the exponential mean failure time.

20. Sequential point estimation of the mean residual life under random censorship.

21. Fixed-width confidence intervals for the regression parameters in linear models under censorship.

22. Sequential estimation of the regression parameter in the Cox Model.

b) List of Invited Colloquia, Conferences and Seminars;

Joseph C. Gardiner, Principal Investigator

The results of our research efforts performed under Contract N00014-17-C-0522 were presented at the following professional gatherings.

1. Symposium on Adaptive Statistical Procedures and Related Topics, Brookhaven National Laboratories, New York (1985).

2. Institute of Mathematical Statistics, Eastern Regional Meeting, Stony Brook, New York (1985).

3. Department of Biostatistics, Columbia University, New York (1985).

4. Department of Statistics, Colorado State University, Fort Collins (1985).

5. GTE Laboratories, Waltham, Massachusetts (1984).

6. Department of Applied Mathematics and Statistics, State University of New York, Stony Brook, New York (1984).

7. Statistics Center, Cornell University, Ithaca, New York (1984).

8. Department of Statistics and Biostatistics, University of North Carolina, Chapel Hill, North Carolina (1984).

9. Department of Statistics, Oklahoma State University, Stillwater, Oklahoma (1983).

10. American Statistical Association and Institute of Mathematical Statistics, Joint Meeting, Toronto, Canada (1983).

11. Department of Mathematical Sciences, State University of New York, Binghamton, New York (1982).

12. Department of Mathematical Statistics, Columbia University, New York (1982).

13. Biometric Society (ENAR), San Antonio, Texas (1982).

14. Special Topics Conference on Survival Analysis, The Ohio State University, Columbus, Ohio (1981).

15. Conference on Reliability and Maintainability Office of Naval Research and Army Research Office, Washington, D.C. (1981).

c) Description and significance of research accomplished under Contract N00014-17-C-0522

Joseph C. Gardiner, Principal Investigator.

We shall briefly review here the results obtained in the 16 publications listed in (a) and indicate their contribution to statistical theory and methodology. Our discussion is presented under the following rubrics.

i) Introduction

ii) Sequential Inference Procedures with censorship data

iii) Likelihood ratio processes in progressively censored data

iv) Biometric functional estimation in multiple decrement models

i) Introduction.

Our research effort has been in the broad area of statistical analyses with censored or incomplete data. The basic statistical model entails observation of a lifetime X or its competing censoring time Y, whichever comes first, for each unit in a sample of specimens. The term "lifetime" is given a broad interpretation and includes such examples as the time to failure of a mechanical or an electronic component as in a reliability study, or the survival time of a laboratory specimen as in a clinical study or the duration to some specific end point as in a demographic or epidemological investigation. In these situations it is often the case that the duration variable X of interest is detered from complete observation due to the presence of censorship. Examples include withdrawals from study in clinical and iatrogenic trials and the partial removal of units from testing in a reliability study. The censoring time Y may be stochastic or fixed, but the investigator has to be content to work with the data $Z=\min(X,Y)$ and the identifier $\delta=1$ or 0

according as whether failure preceded censoring or not. For a sample of n specimens therefore, we have the data $\{(Z_i,\delta_i): 1\leq i\leq n\}$. In the random censorship model one assumes the X_i,Y_i are independent random variables, that is, the censoring mechanism is noninformative.

In several longitudinal studies the variables $\{Z_i;\ 1\leq i\leq n\}$ are themselves time-ordered; the first observation to be recorded is the smallest one $Z_{(1)}$ together with its identifier δ_1^* which is 1 or 0 according as $Z_{(1)}$ is an uncensored or censored observation. This is followed by the next smallest observation $Z_{(2)}$ (together with δ_2^*) and so on until the pair $(Z_{(n)},\delta_n^*)$ is recorded last. It is often the case that prolonged observation may be necessary before the entire sample of observations $\{(Z_{(i)},\delta_n^*):\ 1\leq i\leq n\}$ has been recorded. Limitations on time or economic considerations, let alone ethical reasons, preclude extended periods of experimentation and therefore curtailment of observation at an intermediate stage is generally warranted. If observation is ceased at the k_n-th stage where $k_n\varepsilon\{1,2,\ldots,n\}$ may be a stopping time--an integer-valued stochastic variable such that $[k_n=t]$ depends only on information $\{(Z_{(i)},\delta_i^*):\ 1\leq i\leq t\}$ gathered up to that stage--then the investigator has to deal with the recorded data $\{(Z_{(i)},\delta_i^*):\ 1\leq i\leq k_n\}$. Such data will be called progressively censored data and statistical analyses based on them are necessarily more complicated and subtle due to ordering and dependence among the variables.

The basic statistical model we have described here can be extended to a more general competing risks or multiple decrement model where data of the type (X,J) are gathered. Here once again X denotes the duration variable to some end point, say failure, while J labels the cause of failure or decrement. The random censorship model may be regarded as a

special case in which there are two causes of decrement, true failure or censoring, and X is replaced by Z as before. In the terminology of a competing risks model the variables X,Y are called latent variables.

ii) Sequential Inference Procedures with censored data.

The consideration of large sample sizes is often inappropriate in several reliability and lifetesting situations where economy of time and high per unit costs of units preclude implementation of statistical procedures which require relatively large sample sizes for their proper utilization. In this respect our publications (1,2,4,17) address the question of efficient estimation, in a sense to be made precise here later, of some functionals of the underlying failure distribution. To describe our results suppose we have placed $n(\geq 1)$ homogeneous units on test and record as time elapses the true failure times X_i or the censoring time Y_i, whichever comes first for each unit. We wish to estimate some functional $\theta=\theta(F)$ of the failure distribution $F(=P[X>\cdot])$ based on the accumulated progressively censored data $\{(Z_{(i)},\delta_i^*): 1\leq i\leq k_n\}$ up to stage k_n, where k_n is an appropriate stopping time. Let $b(>0)$ be the per unit cost of an unit placed on test and $c(>0)$ be the per unit cost of time or test. At stage k, the total time on test (TTT) $V_{n,k}$ is given by

$$(2.1)\quad V_{n,k}=\sum_{i=1}^{n} Z_{(i)}+(n-k)Z_{(k)} \quad .$$

Suppose $n=n(c)$ units are placed on test and $\hat{\theta}_{n,k}$ is the current estimate of θ while the estimation error is measured by squared error $(\hat{\theta}_{n,k}-\theta)^2$. Then we may be taking the loss incurred in estimating θ by $\hat{\theta}_{n,k}$ at stage k as

$$(2.2)\quad L_{n,k}=a(\hat{\theta}_{n,k}-\theta)^2+bn+c\,V_{n,k}$$

where $a(>0)$ is a known constant. Then the natural objective is to minimize the expected loss (=risk), $R_{n,k}=EL_{n,k}$ with respect to k, for

given (n,b,c). We have investigated this problem in (4) where we assume θ is the exponential mean failure time and the censoring distribution is unknown but independent of the failure distribution G. The maximum likelihood estimator of θ at stage k is $\hat{\theta}_{n,k}=V_{n,k}/\delta_{n,k}$, where $\delta_{n,k}=\sum_{i=1}^{n}\delta_i^*$. Assuming $\lim_{c\downarrow 0} cn^2=a^*\epsilon(0,\infty)$, $b=\rho c$ it is shown that along sequences $\{k_n\}$ for which $n^{-1}k_n\to\lambda$, $\lambda\epsilon(0,1]$, the risk

$$(2.3)\quad R_{n,k_n}=(a\theta^3/b_\lambda)k_n^{-1}+\rho cn+cb_\lambda k_n+o(k_n^{-1}) \quad \text{where} \quad b_\lambda=\lambda^{-1}\int_0^{H^{-1}(\lambda)}H(x)dx\ ;$$

$H'(o)b(o)=-1$ and $H=FG$. In this situation the optimal choice of k_n is the integer k_c^o closest to $(a\theta^3/cb_\lambda^2)^{\frac{1}{2}}$, if $a^*>a\theta^3(EZ)^{-2}$ and n otherwise. In the later case observation continues until all units have responded. It can be shown that $R_{n,k}$ an be optimized only along sequences $\{k_n\}$ for which $n^{-1}k_n\to\lambda$, $\lambda\epsilon(0,1]$. As $c\to 0$ notice that $n^{-1}k_c^o\to\lambda$, provided λ is a solution of

$$(2.4)\qquad \int_0^{H^{-1}(\lambda)}H(x)dx=(a\theta^3/a^*)^{\frac{1}{2}}$$

Since both λ,θ are unknown the specification of the optimal <u>stopping number</u> k_c^o cannot be made. We explore an analogous sequential procedure which ceases observation at the random stopping stage N_c and consequently estimates θ by $\hat{\theta}_c=\hat{\theta}_{n,N_c}$. Defining

$$(2.5)\quad N_c=\begin{cases}\min\{k\le n-1:\ \hat{\theta}_{n,k}^3\ge (a/c)V_{n,k}\}\\ n\ ,\ \text{if no such } k \text{ exists}\end{cases}$$

it is shown that the sequential estimation scheme $(N_c,\hat{\theta}_c)$ behaves as good as the "fixed-sample" scheme $(k_c^o,\ \hat{\theta}_{n_c o})$ with regard to their risk. If $R_c^*=EL_{n,N_c}$ is the risk of the sequential procedure and R_c^o is the corresponding optimal risk of the procedure $(k_c^o,\ \hat{\theta}_{n_c o})$ then $R_c^*/R_c^o\to 1$ as $c\downarrow o$, that is,our scheme is <u>asymptotically risk-efficient.</u>

Furthermore $N_c/k_c^o \to 1$ and $\hat{\theta}_c$ properly normalized, has the limiting normal distribution.

Our publication (4) is the first attempt in obtaining a risk efficient time sequential scheme for the estimation of the mean exponential failure time when the observations are subject to censorship.

The results of Sen (1981), in which censorship is absent, can be obtained as a special case. The quintessence of our arguments is the derivation of (2.3). In the absence of censoring, $\hat{\theta}_{n,k}=k^{-1}V_{n,k}$ and since $V_{n,k}$ of (2.1) is then the sum of k independent exponential random variables with mean θ, $R_{n,k}$ takes a particularly simple form. The technical machinery brought to play in the case of censorship involved certain inequalities for martingales both in discrete and continous time, convergence of sequences of dependent random variables and the moments of normalized empirical processes. We believe that some of these tools are also new.

In publications (1) and (3) the parallel problems of risk-efficient estimation of θ and fixed width interval estimation are analysed. In (1) the loss structure is simpler, $L_{n,n}=a(\hat{\theta}_{n,n}-\theta)^2+bn$ and we focus on minimizing the recruitment sample size $n=n(b)$ of units for a given per unit cost b. In (3) the objective is to obtain a confidence interval for θ of given width $2d$ having a prescribed <u>coverage probability</u> $(1-\alpha)$. Since $\hat{\theta}_{n,n}=V_{n,n}/\delta_{n,n}$ is the maximum likelihood estimate of θ based on $B_{n,n}$, $\{n^{\frac{1}{2}}(\hat{\theta}_{n,n}-\theta); n\geq 1\}$ has limiting normal distribution $N(o,\sigma^2)$ a natural candidate for a confidence interval for θ of width $2d$ is $I_n=[\hat{\theta}_{n,n}-d, \hat{\theta}_{n,n}+d]$. By taking a sample size $n=n(d)$ of at least $(z_{\alpha/2}\sigma/d)^2$ we can guarantee

$$\lim_{d\to o} P_\theta[I_n \varepsilon \theta] \geq 1-\sigma \quad \text{for all} \quad \theta$$

However, since σ^2 is unknown, depending on θ and the unknown censoring distribution, the specification of $n(d)$ cannot be made. We propose a sequential scheme in (3) that takes $N=N(d)$ observations such that the resulting confidence interval $I_{N(d)}$ is <u>asymptotically consistent and efficient</u>, that is as $d \to o$ and all θ,

$$\lim P_\theta[\theta \epsilon I_N] = 1-\alpha$$

and

$$\lim E_\theta\{N(d)\}/n(d)=1 \ .$$

If the underlying failure distribution is also left unspecified, then problem of efficient estimation of the mean failure time becomes considerably more difficult. We have addressed this problem in (2) and in the case of median failure time in (5) and (17). The estimates chosen here are functionals of the product limit estimator of F.

The techniques developed here hold much promise in solving some related problems which we shall examine in our future research.

In addition to the optimality property of asymptotic risk-efficiency in the point estimation case and of asymptotic consistency and efficiency in the interval estimation case an investigation of an higher order of optimality becomes necessary in certain situations. The basic problem of efficient estimation of the median failure time is taken up in (16, 18, 19). A bounded length interval estimation scheme is one in which sampling is curtailed upon achievement of a desired prespecified width of the random interval under utilization. The fixed-width design described earlier always maintains a constant (fixed) width throughout sampling.

In publication (18) we find that both these procedures are asymptotically consistent and efficient. Therefore theoretical development of expansions for the coverage probability and of expected sample size will be needed to differentiate between these schemes. A simulation study under investigation at present has shed some light as to which procedure will be better. The current simulations carried out by the investigator point to the bounded length procedure, in a particular setting, as appropriate for moderate sample sizes. The problem is being investigated further.

iii) Likelihood ratio processes in progressively censored data.

The property of local asymptotic normality (LAN) for a family of probability measures is of fundamental importance in the asymptotic theory of estimation and hypothesis testing. A comprehensive examination of sets of conditions ensuring the LAN property for various families of probability distributions can be found in LeCam (1960). Numerous applications are available in Roussas (1971) and Ibragimov and Has'minskii (1981). Attention has been focussed on families of distributions connected with a sequence of independent random variables or those associated with a homogeneous Markov chain. For the progressively censored data $\{Z_{(i)};\ 1 \leq i \leq k_n\}$ the variables are neither independent nor identically distributed. In (9)

this LAN property is derived for a wide class of parametric failure distributions and some applications to estimation are described. Suppose the underlying variable Z has distribution involving the parameter θ and corresponding to $\{Z_{(i)}: 1\leq i\leq k_n\}$ form the likelihood ratio statistics

$$\Lambda_{n,k}(\theta,\theta_n) = p(\underset{\sim}{Z}_{(k)};\theta_n)/p(\underset{\sim}{Z}_{(k)},\theta), \qquad 1\leq k\leq n$$

where $p(\cdot;\theta)$ denotes the joint density of $Z_{(k)}=(Z_{(1)},\ldots,Z_{(k)})$. As described earlier expermentation may be curtailed at a (random) stage k_n depending on the accumulated data and so it is instructive to examine the stopped statistics Λ_{n,k_n}. Under certain conditions of regularity on the underlying response distribution we obtain with $\theta_n=\theta+un^{-\frac{1}{2}}$,

$$(2.6) \quad \Lambda_{n,k_n(t)}(\theta,\theta_n)=\exp\{uJ_\alpha^{\frac{1}{2}}(\theta)W(t)-\tfrac{1}{2}u^2tJ_\alpha(\theta) + \ell_n\}$$

where $t\to k_n(t)$, $t\in[0,1]$ are certain (random) integer valued functions. $t\to W(t)$ is Brownian Motion in the space $D[0,1]$ and ℓ_n a remainder negligible in probability. The expansion (2.6) may be called the LAN property and itsimportance lies in the fact that tests of hypothesis of the likelihood ratio type (for contiguous hypotheses) can be constructed and their properties determined by well known properties of the process W. In (9) we have extended to the progressively censored case some results in Ibragimov and Has'minskii (1972, 75) Phillipou and Roussas (1973) and Inagaki and Ogata (1977). For a special class of survival distributions weak convergence of progressively censored likelihood ratio processes in $D[o,\infty]$ is illustrated in (10).

iv) Biometric functional estimation in multiple decrement models.

In many survival analyses, as in clinical trials and lifetesting, estimation of the underlying survival distribution is of fundamental

importance since it summarizes the mortality experience of the items or specimens under study. In the case of censored data the estimator of the failue curve $t \to F(t)(=P[X>t])$ of common use is the celebrated product-limit estimator. Based on the data $\{(Z_i,\delta_i): 1\leq i\leq n\}$ this estimator can be expressed in the form

$$(2.7) \qquad F_n(t) = \prod_{i=1}^{n} \{\frac{N(Z_i)}{1+N(Z_i)}\}^{[Z_i\leq t,\ \delta_i=1]} \quad ;\ t\geq 0$$

where the exponent denotes the indicator function of the event in parenthesis. Here $N(t) = \sum_{i=1}^{n} [Z_i > t]$ is the number of items at risk at time t. The properties of $t \to F_n(t)$ has been the subject of intensive research in recent times (Gill (1983)). In (8) we have addressed the question of estimation of the failure curve when the investigator has at his disposal only progressively censored data of the type $\{(Z_{(i)}, \delta_i^*): 1\leq i\leq k_n\}$. The approach adopted here is a Bayesian one where, by imposing a Dirchlet process prior on F and using a weighted squared-error loss, an appropriate generalization to the progressively censored case of an estimator of F given by Susarla and van Ryzin (1976) is obtained. We also note that our estimator in (8) encompasses both fixed and random censorship. It includes, of course, the cases in which the complete sample is observed $(k_n=n)$, an extension of an estimator of Ferguson (1973) when no censoring is present and the product-limit estimator (2.7). The asymptotic theory of our non-parametric Bayesian estimate of F is discussed in (7).

As noted in the Introduction the competing risks model entails observation on data of the type (X,J) where X plays the role of a duration variable, such as failure time and J an index labelling the cause of failure. Central to some epidemological and demographic studies is the

evaluation of certain incidence rates (fertility rates, mortality rates, etc.) which may be expressed in terms of the failure distribution $t \to F(t)=P[X>t]$ and the cause-specific failure rate functions $\{g_i\}$ given by

$$(2.8) \qquad g_i(t) = \lim_{\Delta t \to 0} P[t<X\leq t+\Delta t,\ J=i \mid X>t]/\Delta t.$$

Thus g_i may be interpreted as the instantaneous probability of failure by decrement "i" at time t, given survival up to t from all risks. On the assumption that $c(\geq 1)$ mutually exclusive risks are operative it is easily seen that

$$(2.9) \qquad F(t)=\exp\left(-\sum_{i=1}^{c} \int_0^t g_i(x)dx\right).$$

The occurrence-exposure rate corresponding the decrement "i" is defined as the functions $\alpha_i(t)$ where

$$(2.10) \qquad \alpha_i(t)=\int_0^t g_i(x)F(x)\,dx \Big/ \int_0^t F(x)\,dx$$

This can be re-expressed as $P[X\leq t,\ J=i]/E(Xt)$ and therefore $\alpha_i(t)$ has been interpreted as the mean mortality risk by decrement i over the duration $[0,t]$. In (14) the estimation of the $\{\alpha_i\}$ is addressed and the asymptotic distribution of empirical occurence-exposure rates is obtained. It is noted that in (14) our formulation is only in terms of observable entities. We do not introduce conceptual failure times, one for each type of decrement, and therefore no ad hoc assumptions are necessary on their joint distribution. This averts the identifiability problems that arise in this connection. An interesting consequence of our theory is that the empirical occurrence-exposure rates are in general asymptotically correlated with the sign of this correlation related to the monotonicity of the cause-specific failure rates of the individual

risks (when all risks are operative). We have cited examples where this correlation is zero, thereby ensuring at least asymptotically, independence between rates. In (15) a more elaborate view is taken by examining the behavior of the process of empirical occurrence-exposure rates in the space $D^C[o,\infty)$.

REFERENCES

Ferguson, T. (1974). A Bayesian analysis of some nonparametric problems. Ann. Statist. 1, 209-230.

Gill, R. (1983). Large sample behavior of the product-limit estimator on the whole line. Ann. Statist. 11, 49-58.

Ibragimov, I. and Has'minskii, R. (1981). Statistical Estimation. Springer-Verlag.

Ibragimov, I. and Has'minskii, R. (1972). Asymptotic behavior of statistical estimators in the smooth case. I. Study of the likelihood ratio. Theory Probab. Appl. 17, 445-462.

Ibragimov, I. and Has'minskii, R. (1975). Local asymptotic normallity for non-identically distributed observations. Theory Probab. Appl. 20, 246-260.

Inagaki, N. and Ogata, Y. (1977). The weak convergence of the likelihood ratio random fields for Markov observations. Ann. Inst. Statist. Math. A 29, 165-187.

LeCam, L. (1960). Locally asymptotically nomal families of distributions. Univ. Calif. Publ. Statist.

Philippou, A. and Roussas, G. (1973). Asymptotic distribution of the likelihood function in the independent not identically distributed case. Ann. Statist. 1, 454-471.

Roussas, G. (1972). Contiguity of Probability Measures: Some Applications in Statistics. Cambridge Univ. Press.

Sen, P.K. (1980). On time-sequential point estimation of the exponential mean. Commun. Statist. 9, 27-38.

Susarla, V. and van Ryzin, J. (1976). Nonparametric bayesian estimation of survival curves from incomplete observations. JASA 61, 897-902.

Concluding Remarks

The principal investigator expresses his thanks to the Office of Naval Research for the support and interest extended in the research performed under this contract.

The statistical methodologies developed under this contract have provided practical and useful extensions of the literature on the analyses of failure time data. Furthermore, this has led to new results in the treatment of censored sequential designs in survival analyses. Our current program of research will address various important early decision rules including curtailed testing procedures that will have impact on statistical practice in several longitudinal studies.

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER	2. GOVT ACCESSION NO. ADA 162703	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) Final Report		5. TYPE OF REPORT & PERIOD COVERED
		6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Joseph C. Gardiner		8. CONTRACT OR GRANT NUMBER(s) N00014-79-C-0522
9. PERFORMING ORGANIZATION NAME AND ADDRESS Michigan State University East Lansing, MI 48824		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
11. CONTROLLING OFFICE NAME AND ADDRESS Statistics and Probability Arlington, VA 22217 —		12. REPORT DATE December 1985
		13. NUMBER OF PAGES 20
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office)		15. SECURITY CLASS. (of this report) Unclassified
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

APPROVED FOR PUBLIC RELEASE: DISTRIBUTION UNLIMITED.

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

DD FORM 1473 EDITION OF 1 NOV 65 IS OBSOLETE

S/N 0102-LF-014-6601

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SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

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